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Declaration under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **DIAGNOSTICS AND THERAPEUTICS FOR DISEASES ASSOCIATED WITH HUMAN G-PROTEIN COUPLED RECEPTOR 14 (GPR14)**

(57) Abstract: The invention provides a human GPR14 which is associated with the hematological diseases, cardiovascular diseases, disorders of the peripheral and central nervous system, urological diseases, endocrinological diseases and cancer. The invention also provides assays for the identification of compounds useful in the treatment or prevention of hematological diseases, cardiovascular diseases, disorders of the peripheral and central nervous system, urological diseases, endocrinological diseases and cancer. The invention also features compounds which bind to and/or activate or inhibit the activity of GPR14 as well as pharmaceutical compositions comprising such compounds.

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INTERNATIONAL SEARCH REPORT

Intern: Application No
PCT, ... 03/11393

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	G01N33/74	A61P7/00	A61P9/00	A61P25/00	A61P13/00
	A61P15/00	A61P35/00			

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, WPI Data, PAJ, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/40192 A (SMITHKLINE BEECHAM LAB ; SMITHKLINE BEECHAM PLC (GB); SMITHKLINE BEECH) 12 August 1999 (1999-08-12) page 19, paragraph 4 - page 21, paragraph 2 page 21, line 19 - line 21 page 24, paragraph 3 - page 29, paragraph 3 page 29, paragraph 3 - page 34, paragraph 3 claims 17-31,33; figures 3,4; examples 4-9 -& DATABASE EBI EMBL; 12 August 1999 (1999-08-12), XP002283829 retrieved from EBI Database accession no. AAY32920 abstract ----- -/-	1-26
X	----- -----	1-26

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

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Date of mailing of the international search report

15 OCT 2004

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Schalich, J

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: claims 1-26 (in part)

Therapeutic and diagnostic use of GPR14 for haematological diseases

2. claims: claims 1-26 (in part)

Therapeutic and diagnostic use of GPR14 for cardiovascular diseases

3. claims: claims 1-26 (in part)

Therapeutic and diagnostic use of GPR14 for disorders of the peripheral nervous system

4. claims: claims 1-26 (in part)

Therapeutic and diagnostic use of GPR14 for disorders of the central nervous system

5. claims: claims 1-26 (in part)

Therapeutic and diagnostic use of GPR14 for urological disorders

6. claims: claims 1-26 (in part)

Therapeutic and diagnostic use of GPR14 for endocrinological disorders

7. claims: claims 1-26 (in part)

Therapeutic and diagnostic use of GPR14 for cancer

INTERNATIONAL SEARCH REPORT

Intern'l Application No
PCT/cr 03/11393

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 1 295 867 A (TAKEDA CHEMICAL INDUSTRIES LTD) 26 March 2003 (2003-03-26) page 36, line 55, paragraphs 8,9 - line 58; claim 31 & WO 02/00606 A (TAKEDA CHEMICAL INDUSTRIES LTD) 3 January 2002 (2002-01-03) the whole document -----	19-21, 24-26
X	& WO 01/66143 A (TAKEDA CHEMICAL INDUSTRIES LTD) 13 September 2001 (2001-09-13) the whole document	19-21, 24-26
P,X	EP 1 262 195 A (TAKEDA CHEMICAL INDUSTRIES LTD) 4 December 2002 (2002-12-04) claims 4-7	19-21
X	----- & WO 01/66143 A (TAKEDA CHEMICAL INDUSTRIES LTD) 13 September 2001 (2001-09-13) the whole document	19-21
A	ELSHOURBAGY NABIL A ET AL: "Molecular and pharmacological characterization of genes encoding urotensin-II peptides and their cognate G-protein-coupled receptors from the mouse and monkey" BRITISH JOURNAL OF PHARMACOLOGY, vol. 136, no. 1, May 2002 (2002-05), pages 9-22, XP002283828 ISSN: 0007-1188 the whole document -----	1-26

INTERNATIONAL SEARCH REPORT

Inte

national application No.
CT/EP 03/11393

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 26 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-26 in part

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 26 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

claim 26:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: -

Present claims 19-21 and 24-26 furthermore relate to compounds defined by reference to a desired characteristic or property, namely to bind to or modulate the activity of G-protein coupled receptor 14 (GPR14). The claims cover all diseases and compounds having said characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such diseases and compounds. Independent of the above reasoning, the claims also lack clarity (Article 6 EPCT). An attempt is made to define the diseases and compounds by reference to a result to be achieved, but no technical features according to Rule 6.3. (b) PCT are given. A skilled person can not reduce to practice definitions as given in said claims, since there exist potentially limitless structural possibilities, comprising structures yet to be made, whereas it is not even possible to distinguish said claims over the state of art, since this would entail testing all known compounds/compositions for said activities (modulating or binding).

Consequently, the search has been carried out for:

compositions referred to in claims 19-21 and 24-26: antibodies, antisense polynucleotides and modulators of said polypeptide, described in the state of the art

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT, ... 03/11393

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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